III. REMARKS

Claim Status

Claims 1-42 are in the case. Claims 14 and 18-22 have been cancelled. Claims 1-10 are in condition for allowance; claims 13, 15-17 and 29-35 stand rejected; claims 1, 9-`11 and 42 have been amended; claims 14 and 28 have been cancelled.

Claim Rejections - 35 USC § 112 1st paragraph Enablement

Claims 13, 15-17 and 29-35 stand rejected under 35 USC § 112, 1st paragraph because the specification, while being enabled for inhibiting Cox-1 and Cox-2 *in vitro*, having analgesic activity *in vivo* in rats, having activity against edema *in vivo* in rats, having anti arthritic activity in rats and showing PGE2 production in rats, the Examiner is of the opinion that the specification lacks enablement for the treatment and/or prophylaxis of diseases and disorders disclosed in claims 13, 15 to 17 and 29 - 35.

Applicant respectfully disagrees with the view held by the Examiner.

The specification in the present case contains pharmacological data which prove the inhibition of COX-1 and COX-2 by the compounds of the presently claimed invention *in vitro* (page 39 and page 40), the analgesic activity of the compounds of the present Invention *In vivo*

(page 40), the activity against edema of the compounds of the present invention *in vivo* (page 41), the antiarthritic activity of the compounds of the present invention *in vivo* (page 0 141) and PGE2 production by the compounds of the present invention in rats (page 42).

Thus, this pharmacological data, in particular the pharmacological data obtained by *in vivo* assays, give clear evidence that the compounds of the present invention can be used in the treatment of COX-1 and/or COX-2 related disorders (claim 13), in the treatment of pain (claim 15), in the treatment of inflammation (claim 16) and in the treatment of inflammation disorders (claim 17).

In addition, Applicant believes it is apparent from the pharmacological data included in the present application that it is also clear that the inventively claimed compounds effectively inhibit COX-1 and/or COX-2.

Furthermore, it is common knowledge among those skilled in the art that compounds acting as inhibitors of COX-1 and/or COX-2 are effective in the treatment of several diseases such as pain and inflammation. This common knowledge is established, *inter alia,* by numerous patents granted by the USPTO. A limited overview of patents that establish a link between the inhibition of COX-1 and/or COX-2 and the claimed diseases is given in the fallowing table.

Claim	Disorder	US Patent
15	Pain	6,310,099; 6,441,014; 6,753,344; 6,822,102; 7,138,411: 6,077,850; 6,451,858
16	Inflammation	6,310,099; 6,441,014; 6,753,344; 6,806,288; 6,822,102; 7,138,411; 6,077,850; 6.743,816; 6.451,858
17	Inflammation disorders including arthritis	6,310.099; 6,441,014; 6.806,288; 6,822,102; 7,138,411; 6,451,858
29	Angiogenesis mediated disorders	6,025,353; 6,686,390; 6,596,736; 6,555,540
30	Cancer	6,310,099; 6,822,102; 7,138,411; 6,077,850; 6,743,816
31	Gastrointestinal disorders	6,846,818; 6,696,477; 6,686,390
32	Skin related disorders	6,440,973; 4,695,586; 6,686,390
33	Bronchitis	6,743,816
34	Fever	6,441,014; 6,753.344; 6,806,288; 6,743,816
35	Polyps	6,743,816

With respect to the cited literature, please note that it is thus reasonable to expect that the compounds of the present invention that effectively inhibit COX-1 and/or COX-2 can be used in the treatment of the disorders as claimed in claims 15-17, and 29-35.

In addition, the specification provides working guidance for those skilled in the art how to prepare the compounds of the present invention (pages 26 to 38) and how to administer the compounds of the present invention (pages 19 and 20). In particular, specific ED50 values are given for the administration of compounds in the analgesia test, in the test for activity against edema and in the test for

anti-arthritic activity (pages 40 and 41). Hence, those skilled in the art are able to calculate the required amount to effectively treat the disorders disclosed in the present invention,

Applicant respectfully suggests that the Examiner's request to provide additional experimental data as for, *inter alia*, a specific protocol for the administration of the compounds of the present invention and the bioavailability, formulation and stability of the compounds of the present invention is not required in order to enable a person skilled in the art to carry out the present invention. This is even truer since those skilled in the art are familiar with common ways of administration of pharmaceutical compounds.

In addition, Applicant believes that the Examiner's request to provide additional experimental data for the present application is unjustified and not in accordance with prevailing US practice. The revision of experimental data on the bioavailability, formulation, stability and the like of a certain compound is a matter of regulation for the Food and Drug Administration to handle and is not appropriate in the context of an examination within the patent office. Hence, a lack of disclosure of these data should not be relevant to nor should it be disadvantageous to the patentability of the presently claimed invention.

Furthermore, the Examiner asserts that it is known to those skilled in the art that COX-1 and COX-2 inhibitors cause ulceration and show toxicity. Assuming, *arguendo*, that the

examiner is correct and that ulceration can be caused when using COX-1 and COX-2 inhibitors in high doses for a long term, this effect is not relevant to the question of the general activity of the compounds of the presently claimed invention in the treatment of COX-1 and/or COX-2 related disorders.

Again, in this respect the evaluation of possible negative side effects of pharmacologically active compounds is not a matter of the USPTO but rather of the Food and Drug Administration. Thus, the occurrence of potential side effects should not be prejudicial to the general patentability of the present invention.

In summary, applicant respectfully suggests that the standard set by the Examiner to fulfill the necessary requirements for enablement is inappropriately high and takes into consideration elements that are not pertinent to a patentability examination before the USPTO. Requirements such as those proposed by the examiner are excessive and not germane to the issue of patentability.

Applicant reserves the right to file divisional applications for any subject-matter that has been deleted the application as originally filed.

The Commissioner is hereby authorized to charge payment for any fees associated with this communication or credit any over payment to Deposit Account No. 16-1350.

Respectfully submitted,

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